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Review Article

Thiazoles: A Valuable Insight in to the Recent Advances and Biological Activities

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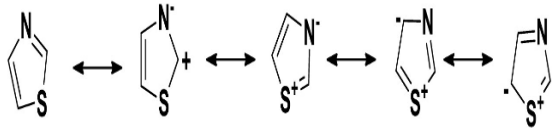
Abstract:

The heterocycle thiazole, which consists of Sulfur and Nitrogen atoms, plays a significant role in the study of medicine. Thiamine (Vitamin B1) and many other naturally occurring and synthetically produced substances of therapeutic significance have this core scaffold. The penicillin nucleus, of which thiazole is a crucial component, and some of its derivatives have showed antibacterial (sulfazole), antiretroviral (ritonavir), antifungal (abafungin), antihistamine, and antithyroid properties, demonstrating the flexibility of the thiazole nucleus. Recent uses as an anticancer (tiazofurin) and anthelmintic have greatly boosted the synthetic relevance of thiazole derivatives, its reduced forms, and condensed derivatives.

Key words: Thiazoles derivatives; Biological activities..

INTRODUCTION

The nitrogen and sulfur atoms in thiazole make it a heterocyclic molecule with an aromatic five-membered ring. Nitrogen plus one additional heteroatom in a five-membered ring are termed 1, 3-azoles, which includes thiazole and similar compounds. Isomers of the 1, 2-azoles, isothiazole is a nitrogen-sulfur chemical. Thiazole derivatives
may be named using the convention shown in the table below.

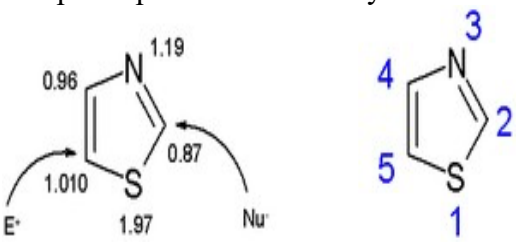


Thiazole, also known as 1,3-thiazole, is a heterocyclic molecule consisting of sulfur and nitrogen; the name 'thiazole' may also refer to a vast family of derivatives. Thiazole has the chemical formula C3H3NS and appears as a colorless to light yellow liquid with a scent reminiscent to pyridine.[1]

The azoles, which also contain imidazoles and oxazoles, are a class of heterocycles that includes thiazoles. The thiazole group is another kind of functional group. Oxazoles are similar molecules where oxygen takes the place of sulfur. The sulfur in thiazoles

has been replaced by nitrogen, making them structurally similar to imidazoles.

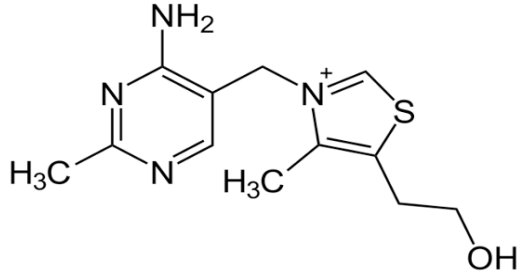
The aromatic ring structure of thiazoles is flat. The aromaticity of thiazoles is higher than that of equivalent oxazoles because of their increased pi-electron delocalization. The chemical shift of the ring protons (between 7.27 and 8.77 ppm) in proton NMR spectroscopy is indicative of the aromaticity and the presence of a robust diamagnetic ring current. C5 is the predominant site for electrophilic substitution while C2 is the primary site for nucleophilic substitution, as shown by the computed pi- electron density.



Thiazole is aromatic on the basis of delocalization of a lone pair of electrons from the sulfur atom completing the needed 6 π electrons to satisfy Huckel's rule. The resonance forms are

The p-bond orders quantified by molecular orbital methods have specified thiazole molecule to be aromatic with some dienic nature. Localization energies have projected reducing order of the nucleophilic reactivities following the order: 2 > 5 > 4 and the electrophilic reactivities as: 5 > 2 > 4. Three hydrogen atoms present in the thiazole are anticipated to have the order of acidity as H2 >> H5 > H4.

Thiazole ring is found naturally in the essential vitamin B1 (thiamin).



Thiamin is a B vitamin that aids in the metabolism of carbohydrates, allowing the body to use them as a source of fuel. As a cofactor in the manufacture of the neurotransmitter acetylcholine, it also contributes to the health of the nervous system. Pasta and refined wheat breads are the most common dietary sources of thiamin. It's also in canned beans like navy and kidney, as well as ready-to-eat cereals.

LITERATURE REVIEW

Vinuta Kamat, Rangappa Santosh, Boja Poojary, Suresh P. Nayak (2020), The design, synthesis, and spectral characterization of a novel family of compounds involving a C(O)-NH-connection to pyridine and thiazole moieties are described. The antibacterial and anti-inflammatory effects of the newly described compounds were tested. These compounds were tested for their anti-inflammatory effects in vitro using the denaturation of bovine serum albumin as a biomarker, and their IC50 values ranged from 46.29 to 100.60 g/mL. Compound 5l has the highest IC50 value of all the chemicals examined, whereas compound 5g has the lowest. The antimicrobial data indicated that compound 5j had the lowest MIC values, whereas compound 5a had the highest. The active compounds also showed improved docking scores and protein-protein interactions when subjected to molecular docking. All of the compounds' mentioned physicochemical properties were determined to be within the acceptable reference range. Their COX-inhibiting effect was discovered by an in-silico molecular docking analysis. The synthesized analogues were tested for their bioactivity, and compound 5j stood out as a major player.

(Demokrat Nuha, Asaf Evrim Evren, Meral Ylmaz Canklc, & Leyla Yurttaş, 2021), Considering 6-acetyl penicillanic acid (6-APA), nine novel thiazole derivatives were

synthesized and tested for antibacterial activity. Using a two-step synthetic approach based on traditional Hantzsch thiazole synthesis, we were able to get the ethyl 2-(2-mercaptoacetamido)-4-methylthiazole-5-carboxylate derivatives (3a-3i). 1H-NMR, 13C-NMR, and HRMS spectrum data were used to determine the compounds' structures. The MIC for each chemical was obtained by testing it on eleven bacterial and sixteen fungal species. High antimicrobial activity was demonstrated by compounds 3d (4-methyl-2-(2-((5-methyl-1,3,4-thiadiazol-2-yl), 3f (4-methyl-2-(2-((5-nitro-1H-benzimidazol-2-yl), and 3g (4-methyl-2-(2-((5-methyl-4H-1,2,4-triazol-3-yl), all of which contained thiazole rings. In silico calculations of the compounds' physicochemical characteristics revealed that they meet the criteria for medication availability.

Lemilemu, F., Bitew, M., Demissie, T.B. *et al.* (2021), Many metabolic enzymes can be modulated by thiazole-based Schiff base molecules, which explains their promising pharmaceutical potential. They've also been shown to be effective against bacteria, fungi, inflammation, free radicals, and proliferation. Thiazole-based Schiff base molecules were synthesized utilizing both traditional and environmentally friendly methods, with ZnO nanoparticles serving as catalyst. The antibacterial and antioxidant properties of the produced compounds ranged from moderate to high. Compound 11 was proven to be an effective antibacterial therapeutic agent against E. coli using in vitro antibacterial activity and molecular docking research, whereas compounds 7 and 9 were revealed to be effective antioxidant agents. Synthesis of physiologically active chemicals was also discovered to be much facilitated by the green synthesis methodology using ZnO nanoparticles as catalyst.

Kumar, S., S.L. Khokra, and A. Yadav. (2021), The substantial biological and pharmacological capabilities of heterocyclic compounds and their derivatives have lately gained a great deal of attention in medicinal chemistry, as documented by a huge number of publications. One of the most significant heterocycles, the triazole nucleus is present in many naturally occurring and pharmaceutically active compounds. Most pharmaceuticals include high amounts of heterocyclic nitrogen. Using the phenomenon of bio-isosteres, in which the oxygen atom of the oxadiazole nucleus is replaced by a nitrogen triazole homologue, the triazole ring is derivatized. These pharmacological actions include, but are not limited to, antibacterial, anticonvulsant, anti-inflammatory, analgesic, antitubercular, anthelmintic, antioxidant, antimalarial, antiviral, and many more. This study focuses on the most up-to-date synthesis technique of the triazole moiety. This article summarizes the current research on triazole compounds that have been shown to have many pharmacological effects. According to the reviewed literature, triazole is the chemical with the highest potential applications.

Arshad, M.F.; Alam, A.; Alshammari, A.A.; Alhazza, M.B.; Alzimam, I.M.; Alam, M.A.; Mustafa, G.; Ansari, M.S.; Alotaibi, A.M.; Alotaibi, A.A.; et al. (2022), The thiazole moiety is a heterocycle that has been used extensively in the chemical industry for decades. The thiazole ring is composed of sulfur and nitrogen in such a way that the pi () electrons are unconstrained and may hop from one bond to another, giving the ring aromatic characteristics. Due to its aromatic nature, the ring has several reactive sites that may participate in donor-acceptor, nucleophilic, oxidation, and other types of reactions. When introduced into biological systems, molecules with a thiazole ring exhibit unpredictable behavior and cause a

different reset. The metabolic processes and enzymes, as well as the stimulation and blocking of receptors, may be affected by these compounds. In order to create new therapeutic agents for a wide range of clinical disorders, medicinal chemists have been concentrating on thiazole-containing molecules. This article aims to educate readers on the three main categories of compounds containing the thiazole group: thiazole-based therapy therapies, thiazole-based clinical trials, and thiazole-based preclinical and developmental stages. Here, we offer a database of thiazole-containing compounds that have undergone some stage of preclinical or developmental testing, with an emphasis on their short synthetic descriptions and preclinical studies related to structure-based activity analyses. The authors hope that this review will encourage medicinal chemists to pursue novel avenues of inquiry that might one day provide effective therapeutics.

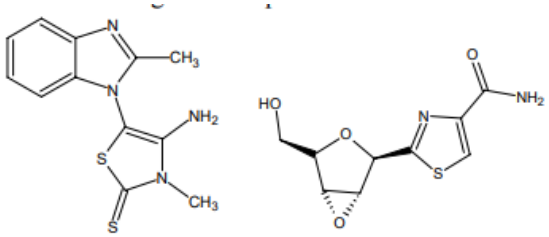
BIOLOGICAL ACTIVITIES

Many powerful physiologically active chemicals, including the antibiotic sulfathiazol, the antiviral medicine ritonavir, the antifungal drug abafungin sold under the brand name Abasol cream, and the antineoplastic drugs bleomycine and tiazofurin, are members of the thiazole family of heterocyclic compounds. Thiazole derivatives have been related with a variety of intriguing biological functions [1-2] for quite some time. Recently, thiazoles have been used as anti-allergic [3], anti-hypertensive [4], anti-inflammatory [5], anti-schizophrenia [6], anti-bacterial [7], anti-HIV [8], hypnotic [9], pain [10], fibrinogen receptor antagonists with antithrombotic activity [11], and new inhibitors of bacterial DNA gyrase B [12] drugs. Below is a quick overview of the many biological functions linked to thiazoles [12].

Antitumor activity

Several 1-substituted-2-methyl-5-nitrobenzimidazoles were produced and tested for anticancer efficacy by Ramla et al. [13]. Compound [1] was discovered to have a notable anti-tumor activity.

Researchers Popsavin et al. [14] presented the results of a screening for anti-tumor activity using a series of 2-(2, 3-anhydrofuranosyl) thiazole-4-carboxamide (2', 3'-anhydro tiazofurin) derivatives. The most potent chemical against K562 cancer cells was compound [2], with IC50 values between 0.09 and 0.49 M. From [6-(4-bromophenyl) imidazol-3yl] acetic acid hydrazide, Gulsory et al. [15] showed a sequence of arylidene hydrazides. The chemicals produced were tested in a primary cytotoxicity assay at a single dosage. On a cell line model of prostate cancer, compound [3] showed the greatest efficacy.



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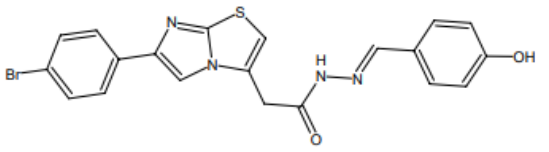
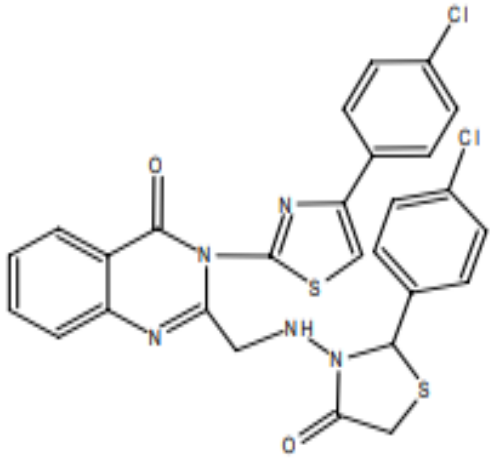


[3]

Anti-inflammatory activity

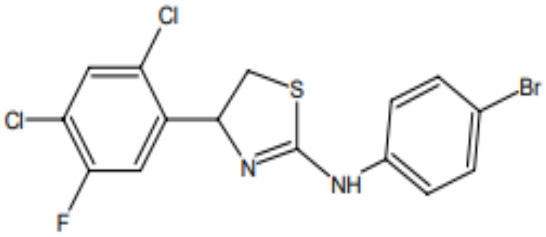
A class of 3-[4'-(p-chlorophenyl) thiazol-2'-yl] was synthesized by Kumar et al.two, [(substituted azetidinone/thiazolidinone)-aminoethy]-6-bromoquinazolin-4-ones and checked for their analgesic and anti-inflammatory properties. High activity in both activities was observed for compound [4]. At a dose of 50 mg/kg po, they discovered that compounds with an added thiazolidinone ring had much higher anti-inflammatory and analgesic action than their

parent compounds. Substituting a chloro group for the phenyl at the second position results in a compound with almost the same anti-inflammatory effect as the gold standard medication phenylbutazone at 50 mg/kg.

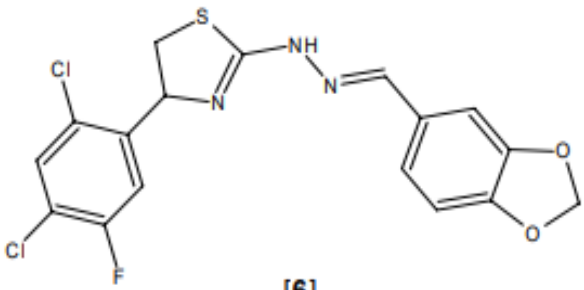


[4]

Holla et al. [17] presented the results of a screening for antibacterial and anti-inflammatory properties performed on a number of series of arylaminothiazoles, arylidene/5-aryl-2-furfurylidene hydrazinothiazoles. The anti-inflammatory effects of two of the newly synthesized compounds [5] and [6] were found to be on par with those of ibuprofen.

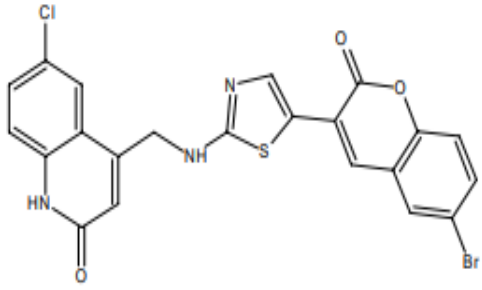


[5]

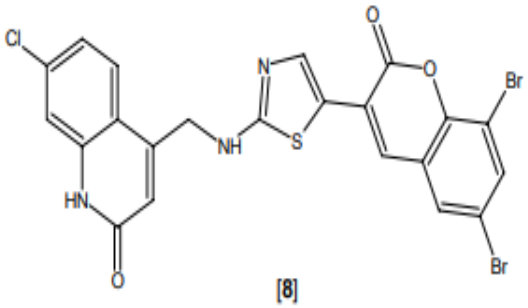


[6]

Kalkhambkar et al. [18] identified coumarin and carbostyril (1-aza coumarin)-containing triheterocyclic thiazoles. In vitro analgesic and anti-inflammatory tests were performed on the newly synthesized drugs. The acetic acid-induced writhing was greatly reduced by [7] and [8], two of the investigated substances.



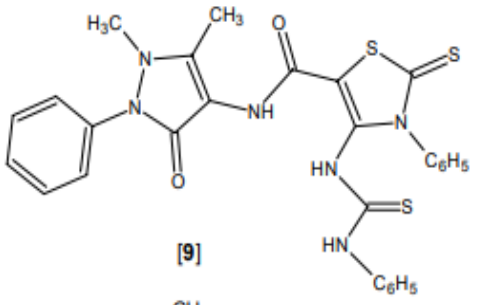
[7]



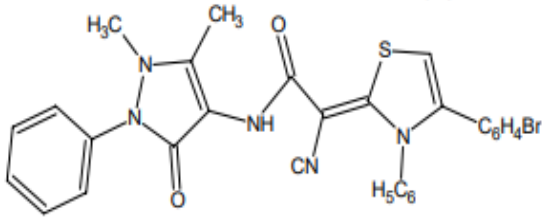
[8]

Hybrid structures with the antipyrine moiety linked to polysubstituted thiazole or 2, 5-disubstituted-1, 3, 4-thiadiazole were described by Rostom et al. [19]. Anti-inflammatory, ulcerogenic, and acute toxic effects of 12 substances were studied. Similar substances were tested for their ability to alleviate pain.

The effectiveness of these substances against microorganisms was also tested in vitro. In addition to their excellent GI safety profile and safety margin, certain compounds [9] and [10] showed outstanding anti-inflammatory and analgesic profiles with rapid start of action. Also, several of the compounds showed efficacy against a wide variety of bacteria.



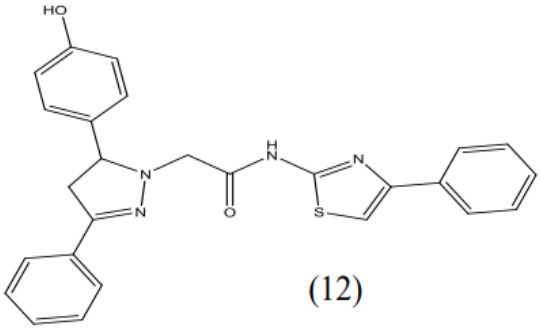
[9]



[10]

Antifungal activity

Through the use of chalcones, novel thiazoles have been synthesized by adding a pyrazole moiety to 2-hydrazinyl-N-(4-phenylthiazol-2-yl) acetamide at the second position.IR, 1H-NMR, Mass spectrum, and Elemental analyses were used to validate the chemical structures of the produced compounds. By using the paper disc diffusion method, these compounds were tested for their antimicrobial (against S. aureus ATCC 9144, S. epidermidis ATCC 155, M. luteus ATCC 4698, B. cereus ATCC 11778, E. coli ATCC 25922, Pseudomonas aeruginosa ATCC 2853, and K. pneumoniae ATCC 11298) and antifungal (against A. Significant antibacterial and antifungal activity were found in several of the synthesized drugs. In terms of antibacterial activity, 2-(5-(4-hydroxyphenyl)-3-phenyl-4,5-dihydropyrazol-1-yl)-N-(4-phenylthiazol-2 yl) acetamide 10 and 2-(5-(4-hydroxy-3-methoxyphenyl)-3-phenyl-4,5-dihydropyrazol-1-yl) acetamide 9 were shown to be the most effective of theThe antifungal activity of compound 32, N-(4-phenylthiazol-2-yl)acetamide, was the greatest.

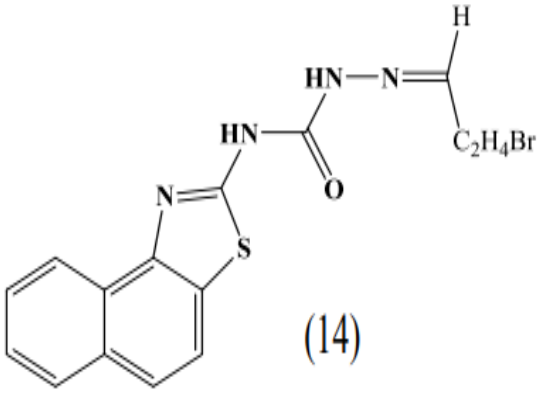


(12)

2-(5-(4-hydroxyphenyl)-3-phenyl- 4,5-dihydropyrazol-1-yl)-N-(4-phenylthiazol-2 yl) acetamide

Anticonvulsant activity:

Azam *et al*. designed and synthesized a series of N^4-(naphtha[1,2-d]thiazol-2-yl)semicarbazides 14 and evaluated fortheir anticonvulsant and neurotoxicity studies.

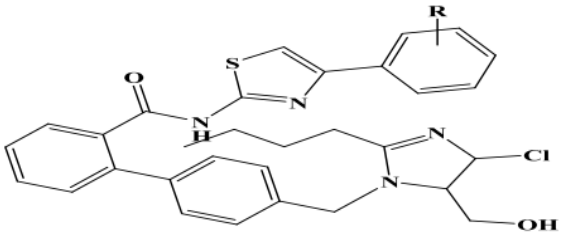


(14)

Antibacterial activity:

The 4'-(2-n-Butyl-4-chloro-5-hydroxymethyl-imidazol-1-yl-methyl-biphenyl-2-caboxylic acid- (4-phenyl/substituted phenyl thiazole)-amide series has been synthesized. We used the cup-plate method with a concentration of 100 g mL-1 on nutrient agar to test compounds for in vitro antibacterial activity against S. aureus and B. subtilis, and we used the same method to test compounds for in vitro antifungal activity against C. albicans and A. niger. The antibacterial effect was tested against DMSO as a solvent control. Antibacterial activity was measured against streptomycin, while antifungal activity was measured against Griesuofulin. Spectral evidence was used to verify the

structures of aminothiazole derivatives. After synthesis, the newly created title compounds were tested for antibacterial activity in vitro. Compounds 15, 16, 17, 18, and 19 showed the most potent antibacterial action. The most effective fungicides found in the screening process were compounds 16, 18, and 19.

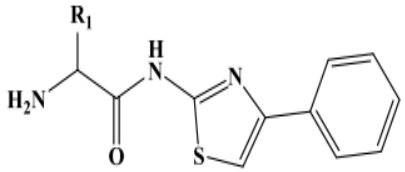


R=Cl,15
F,16
P-OCH_3,17
2,4 (OCH3)2 ,18
2,4(OC2H5)2, 19

Condensation of 2-bromo-1-(4-chlorophenyl) ethanone and thiosemicarbazide in 100% ethanol yielded 1-(5-(4-chlorophenyl)thiazol-2-yl)hydrazine hydrobromide 20 in a single step. Crystallographic data provided unambiguous confirmation of the structure determined using current spectroscopic methods such as FTIR, 1H, and 13C NMR spectroscopy for the target molecule. In vitro antibacterial screening using the agar well diffusion technique revealed that the title chemical was very effective against B. subtilis and S. aureus when compared to the gold standard medication Levofloxacin.

Antihelmintic and insecticidal activity:

Himaja et al.41 used a solution phase approach to manufacture a variety of substituted thiazole containing N-methylated amino acids and peptides 21 and 22 and tested their antihelmintic and insecticidal efficacy. The Garg technique was used to treat earthworms (Eudrilus eugeniea) with an antihelmintic. The synthesized compounds were tested for their insecticidal efficacy against termites (Coptotermis formasanus) using the Morita et al.



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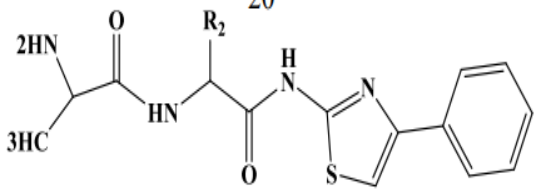
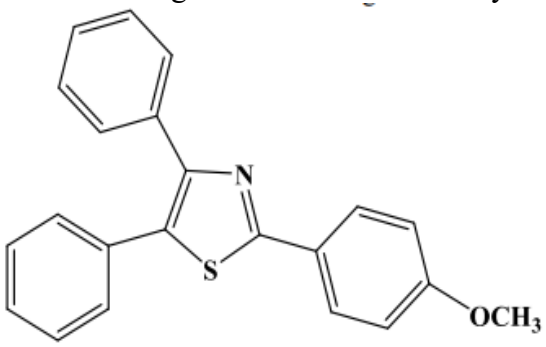


21

Also synthesized the novel compound of thiazole derivative 22. The anthelmintic activity of compounds was tested by utilizing the piperazine citrate as standard and showed a good anthelmintic activity.



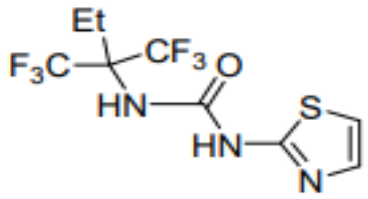
2-(4-methoxyphenyl)-4,5-diphenylthiazole

22

Anticancer activity

Luzina et al.[25] have produced and tested a variety of N-bis(trifluoromethyl)alkyl-N′-thiazolyl and benzothiazolylureas against human cancer cell lines. (32) PC-3 (prostate cancer, log GI50 7.10) and SR (leukemia, log GI50 5.44) human cancer cell lines were the most sensitive to the studied chemical.

Dunn et al.[26] described the synthesis and activity of a series of 4-thiazolyl substituted analogs of new pyrrolocarbazole as inhibitors of poly (ADP-ribose) polymerase-1. The compound 33 was shown to be the most effective of these.



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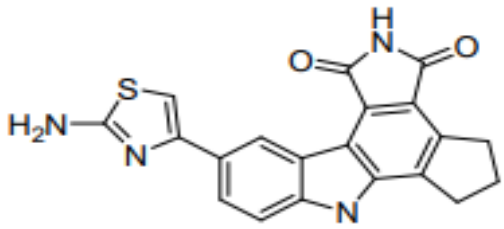

(33)

CONCLUSION

With their diverse biological activity and therapeutic potential, thiazole derivatives have been highlighted as a promising class of chemicals in this study. Based on a review of the relevant literature, we know that thiazole derivatives have a wide range of biological activities, including those with antibacterial, anti-inflammatory, analgesic, antitubercular, anticancer, etc. effects.

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